



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE  
(MBHB Ref. No. 00-816-C (RPI Ref. No. 700.002))

PATENT

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In re Application of: Usman et al.

Serial No.: 09/877,526

Filed: June 8, 2001

For: NUCLEIC ACID SENSOR  
MOLECULES

Group Art Unit: 1634

Examiner: A. Chakrabarti

Confirmation No.: 1423

**RESPONSE TO THE OFFICE ACTION MAILED JULY 12, 2002**

Box Non-Fee Amendment  
Commissioner for Patents  
Washington, D.C. 20231

Dear Sir:

Please consider the following amendments and remarks in response to the Office Action mailed July 12, 2002.

**AMENDMENTS**

**In the claims:**

Please cancel claims 11-14 without prejudice to future prosecution or acquiescence to any rejection.

Please amend claims 9, 10, 15, and 16 to appear as follows (a redlined copy of the amended claims is included herewith):

9. (Amended) A method comprising:

a) contacting

i) a nucleic acid sensor molecule comprising an enzymatic nucleic acid component and one or more sensor components, wherein, in response to an interaction of a single stranded RNA (ssRNA) having a single nucleotide polymorphism (SNP) with the nucleic acid sensor molecule in a system, the enzymatic nucleic acid component catalyzes a chemical reaction on a

**CERTIFICATE OF MAILING (37 C.F.R. 1.8a)**

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Date: October 11, 2002

Michael S. Greenfield

reporter molecule resulting in a detectable response, and wherein the reporter molecule and ssRNA having a SNP are different,

with

- ii) a system comprising at least one ssRNA having a SNP

under conditions suitable for the enzymatic nucleic acid component of the nucleic acid sensor molecule to catalyze a chemical reaction on the reporter molecule resulting in a detectable response; and

- b) assaying for the chemical reaction resulting in a detectable response.

B1  
10. (Amended) A method comprising:

- a) contacting

- i) a nucleic acid sensor molecule comprising an enzymatic nucleic acid component and one or more sensor components, wherein, in response to an interaction of a single stranded DNA (ssDNA) having a SNP with the nucleic acid sensor molecule in a system, the enzymatic nucleic acid component catalyzes a chemical reaction on a reporter molecule resulting in a detectable response, and wherein the reporter molecule and ssRNA having a SNP are different,

with

- ii) a system comprising at least one ssDNA having a SNP

under conditions suitable for the enzymatic nucleic acid component of the nucleic acid sensor molecule to catalyze a chemical reaction on the reporter molecule resulting in a detectable response; and

- b) assaying for the chemical reaction resulting in a detectable response.

15. (Amended) A method comprising contacting

- B2
- a) a nucleic acid sensor molecule comprising an enzymatic nucleic acid component and one or more sensor components, wherein, in response to an interaction of a single stranded RNA (ssRNA) having a SNP with the nucleic acid sensor molecule in a

system, the enzymatic nucleic acid component catalyzes a chemical reaction on a reporter molecule resulting in ligation of a first predetermined RNA molecule to a second predetermined RNA molecule, and wherein the ssRNA having a SNP and the predetermined RNAs are different,

with

- b) a system comprising at least one ssRNA having a SNP

under conditions suitable for the enzymatic nucleic acid component of the nucleic acid sensor molecule to ligate the first predetermined RNA molecule to the second predetermined RNA molecule.

16. (Amended) A method comprising contacting

- a) a nucleic acid sensor molecule comprising an enzymatic nucleic acid component and one or more sensor components, wherein, in response to an interaction of a single stranded RNA (ssRNA) with the nucleic acid sensor molecule in a system, the enzymatic nucleic acid component catalyzes a chemical reaction on a reporter molecule resulting in cleavage of a predetermined RNA molecule associated with a disease, and wherein the ssRNA having a SNP and the predetermined RNA are different;

with

- b) a system comprising at least one ssRNA

under conditions suitable for the enzymatic nucleic acid component of the nucleic acid sensor molecule to cleave the predetermined RNA molecule.

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**REMARKS**

Certain claims have been amended to more clearly define the nature of the claimed invention. In particular, the amended claims have been revised to incorporate the language from the non-elected claims from which they depend. In addition, the phrase "on a reporter molecule" has been added after "catalyzes a chemical reaction" in that language. And, lastly, a phrase "and wherein ... are different" has been added to the end of that language to make clear what was already intended by the claims, i.e., that the molecule that induces the chemical reaction is different from the molecule

involved in the chemical reaction. The applicants believe the amendments merely clarify the scope of what was being claimed all along and do not narrow it any manner.

The applicants affirm their election of Group II, claims 9-16.

Claims 11-14 have been canceled without prejudice to future prosecution or acquiescence to any rejection. The 35 U.S.C. § 102 rejections over Roberston *et al.* and Mitchell *et al.* are therefore rendered moot.

### **Rejection of claims 9-12 under 35 U.S.C. § 103**

Claims 9-12 were rejected as obvious over Robertson in view of Williams. Contrary to the assertions in the Office Action, the combination of Robertson and Williams does not teach the method of the presently claimed invention. Robertson does not teach a nucleic acid sensor molecule comprising an enzymatic nucleic acid component and one or more sensor components, wherein, in response to an interaction of a single stranded RNA (ssRNA) or single stranded DNA (ssDNA) having a SNP with the nucleic acid sensor molecule in a system, the enzymatic nucleic acid component catalyzes a chemical reaction resulting in the ligation of a predetermined RNA molecule to another predetermined RNA molecule. That is, Robertson does not teach chemical reaction catalyzed by an enzymatic nucleic acid molecule on a substrate where the reaction is induced by a single stranded RNA (ssRNA) or single stranded DNA (ssDNA) having a SNP that are distinct from the substrate molecule.

Rather, Robertson simply teaches a method of cleaving a target RNA molecule using an RNA fragment having ribozyme activity derived from hepatitis delta virus. The fragment having ribozyme activity derived from hepatitis delta virus does not comprise an enzymatic nucleic acid component and one or more sensor components, and it does not catalyze a chemical reaction on a substrate in response to a separate single stranded RNA (ssRNA) or single stranded DNA (ssDNA) having a SNP molecule which do not directly participate in the chemical reaction.

Nor does Williams teach chemical reaction catalyzed by an enzymatic nucleic acid molecule on a substrate where the reaction is induced by a single stranded RNA (ssRNA) or single stranded DNA (ssDNA) having a SNP that are distinct from the substrate molecule. Rather, Williams describes a method of sequencing nucleic acid using NTPs and primers for SNP detection. The claimed invention does not require the use of NTPs or sequencing for SNP detection. Williams uses a non-analogous technology for SNP detection that is not applicable to the instantly claimed invention.

Neither Robertson nor Williams provide any implicit or explicit motivation to be combined. Neither Robertson nor Williams teach chemical reaction catalyzed by an enzymatic nucleic acid molecule on a substrate where the reaction is induced by a single stranded RNA (ssRNA) or single stranded DNA (ssDNA) having a SNP that are distinct from the substrate molecule, as presently claimed. Moreover, neither Robertson nor Williams teach ligation reaction catalyzed by an enzymatic nucleic acid molecule as required by the instantly claimed invention. Thus, even were the two references combined as suggested, one would not arrive at the presently claimed methods.

For the foregoing reasons, therefore, the applicants respectfully request reconsideration and withdrawal of this rejection.

### **Rejection of claims 15 and 16 under 35 U.S.C. § 103**

Claims 15 and 16 were rejected as obvious over Long in view of Williams. Contrary to the Examiner's exertion, the combination of Long and Williams does not teach the method of the instant invention. Long does not teach a nucleic acid sensor molecule comprising an enzymatic nucleic acid component and one or more sensor components, wherein, in response to an interaction of a single stranded RNA (ssRNA) or single stranded DNA (ssDNA) with the nucleic acid sensor molecule in a system, the enzymatic nucleic acid component catalyzes a chemical reaction resulting in ligation of a predetermined RNA molecule to another predetermined RNA molecule. That is, Long does not teach chemical reaction catalyzed by an enzymatic nucleic acid molecule on a substrate where the reaction is induced by a single stranded RNA (ssRNA) or single stranded DNA (ssDNA) having a SNP that are distinct from the substrate molecule.

Rather, Long simply teaches a method of ligation of an enzymatic nucleic acid molecule having a hammerhead motif to a separate nucleic acid molecule. Long does not teach a method for ligating RNA molecules using an enzymatic nucleic acid molecule in response to a separate single stranded RNA (ssRNA) or single stranded DNA (ssDNA) having a SNP, where the separate ssRNA or ssDNA do not directly participate in the ligation reaction.

Williams is discussed above, and, as mentioned, it does not teach enzymatic catalysis of a chemical reaction induced by a first molecule not involved in the reaction either. Rather, it describes a method of sequencing nucleic acid using NTPs and primers for SNP detection. The claimed invention does not involve the use of NTPs or sequencing for SNP detection. Simply because Williams technology involves SNP detection does not render all methods of SNP detection as being

obvious. Williams uses a non-analogous technology for SNP detection that is not applicable to the instantly claimed invention.

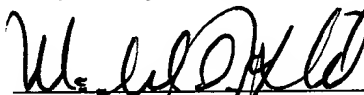
Neither Long nor Williams provide any implicit or explicit motivation to be combined. Moreover, neither Long nor Williams teach separate ssRNA or ssDNA induced ligation of a substrate RNA molecules by an enzymatic nucleic acid molecule, as presently claimed. Thus, even were the two references combined as suggested, one would not arrive at the presently claimed methods.

For the foregoing reasons, therefore, the applicants respectfully request reconsideration and withdrawal of this rejection.

If there the Examiner has any questions or comments regarding this response or the subject application, or if the Examiner believes a teleconference would advance prosecution, the Examiner is invited and encouraged to contact the undersigned.

Date: October 11, 2002

Respectfully submitted,



Michael S. Greenfield  
Registration No. 37,142

Telephone: 312-913-0001  
Facsimile: 312-913-0002

**McDonnell Boehnen Hulbert & Berghoff**  
300 South Wacker Drive, 32<sup>nd</sup> Floor  
Chicago, IL 60606